Subpart F: Inspections and Enforcement of Establishments Described in §1271.10

FDA and the New Paradigm for Tissue Regulation

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Mary A. Malarkey

Director, Office of Compliance and Biologics Quality

Subpart F

- §1271.390 – Applicability
- §1271.400 – Inspections
- §1271.420 – HCT/Ps Offered for Import
- §1271.440 – Orders for Retention, Recall, Destruction, and Cessation of Manufacturing

Applicability: § 1271.390

- "..applicable only to HCT/Ps described in 1271.10 and regulated solely under section 361 of the Public Health Service Act and the regulations in this part and to the establishments that manufacture those HCT/Ps"
- If drugs or devices under the FFDCA, or section 351 products, not subject to these regulations. Held to FFDCA and PHSA 351.
- We received no comments on this section.

Inspections § 1271.400

- General comments:
  - Proposal for third-party inspections
    - Reconsideration in future when have inspectional history on all firms; current resource limitations to start up.
  - Partnering with industry for training
    - Existing practice for investigator training that we hope to continue
  - Special recognition for accredited establishments
    - Agree; has been a consideration for inspectional work-planning and will continue

Inspections
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(a)…you must permit the Food and Drug Administration (FDA) to inspect any manufacturing location at any reasonable time and in a reasonable manner to determine compliance with applicable provisions of this part. The inspection will be conducted as necessary in the judgment of the FDA and may include your establishment, facilities, equipment, finished and unfinished materials, containers, processes, HCT/Ps, procedures, labeling, records, files, papers, and controls required to be maintained under the part. The inspection may be made with or without prior notification and will ordinarily be made during regular business hours.

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- (b) The frequency of inspection will be at the agency's discretion.
- (c) FDA will call upon the most responsible person available at the time of the inspection of the establishment and may question the personnel of the establishment as necessary to determine compliance with the provisions of this part.

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- (d) FDA's representatives may take samples, may review and copy any records required to be kept under this part, and may use other appropriate means to record evidence of observations during inspections conducted under this subpart.
- In response to comments about (c) we clarified that financial records, personnel records (outside or job training) and internal quality audit records will not be reviewed by FDA during inspections.

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- (e) The public disclosure of records containing the name or other positive identification of donors or recipients of HCT/Ps will be handled in accordance with FDA's procedures on disclosure of information as set forth in parts 20 and 21 of this chapter.

HCT/Ps Offered for Import § 1271. 420

- (a) Except as provided in paragraphs (c) and (d) of this section, when an HCT/P is offered for import, the importer of record must notify, either before or at the time of importation, the director of the district of the Food and Drug Administration (FDA) having jurisdiction over the port of entry through which the HCT/P is imported or offered for import, or such officer of the district as the director may designate to act in his or her behalf in administering and enforcing this part, and must provide sufficient information for FDA to make an admissibility decision.

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- (b) Except as provided in paragraphs (c) and (d) of this section, an HCT/P offered for import must be held intact by the importer or consignee, under conditions necessary to prevent transmission of communicable disease, until an admissibility decision is made by FDA. The HCT/P may be transported under quarantine to the consignee, while the FDA district reviews the documentation accompanying the HCT/P. When FDA makes a decision regarding the admissibility of the HCT/P, FDA will notify the importer of record.

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- Revisions made to (a) and (b) from 1270 were to provide clarity and for consistency with agency import policy
- (c) and (d) added due to concerns raised over reproductive HCT/Ps imported under authority of the owner and over potential adverse effects on hematopoietic stem/progenitor cells

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- (c) This section does not apply to reproductive HCT/Ps regulated solely under section 361 of the Public Health Service Act and the regulations in this part, and donated by a sexually intimate partner of the recipient for reproductive use.

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- (d) This section does not apply to peripheral blood stem/progenitor cells regulated solely under section 361 of the Public Health Service Act and the regulations in this part, except that paragraphs (a) and (b) of this section apply when circumstances occur under which such imported peripheral blood stem/progenitor cells may present an unreasonable risk of communicable disease transmission which indicates the need to review the information referenced in paragraph (a) of this section.

Orders for Retention, Recall, Destruction and Cessation of Manufacturing: § 1271.440

- Numerous comments received
  - Concerns about actions being too dramatic and far reaching.
  - Threshold for the actions (violations of GTP vs danger to health)
  - Due Process
  - Five day time frame for recall or destruction
  - Destruction of reproductive HCT/Ps

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- a) Upon an agency finding that there are reasonable grounds to believe that an HCT/P is a violative HCT/P because it was manufactured in violation of the regulations in this part and, therefore, the conditions of manufacture of the HCT/P do not provide adequate protections against risks of communicable disease transmission; or the HCT/P is infected or contaminated so as to be a source of dangerous

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- infection to humans; or an establishment is in violation of the regulations in this part and, therefore, does not provide adequate protections against the risks of communicable disease transmission, the Food and Drug Administration (FDA) may take one or more of the following actions:

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- (1) Serve upon the person who distributed the HCT/P a written order that the HCT/P be recalled and/or destroyed, as appropriate, and upon persons in possession of the HCT/P that the HCT/P must be retained until it is recalled by the distributor, destroyed, or disposed of as agreed by FDA, or the safety of the HCT/P is confirmed;

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- (2) Take possession of and/or destroy the violative HCT/P; or

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- 3) Serve upon the establishment an order to cease manufacturing until compliance with the regulations of this part has been achieved. When FDA determines there are reasonable grounds to believe there is a danger to health, such order will be effective immediately. In other situations, such order will be effective after one of the following events, whichever is later:

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(i) Passage of 5 working days from the establishment's receipt of the order; or

(ii) If the establishment requests a hearing in accordance with paragraph (e) of this section and part 16 of this chapter, a decision in, and in accordance with, those proceedings.

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- (b) A written order issued under paragraph (a) of this section will state with particularity the facts that justify the order.

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- (c)(1) A written order issued under paragraph (a)(1) of this section will ordinarily provide that the HCT/P be recalled and/or destroyed within 5 working days from the date of receipt of the order. After receipt of an order issued under paragraph (a)(1) of this section, the establishment in possession of the HCT/P must not distribute or dispose of the HCT/P in any manner except to recall and/ or destroy the HCT/P consistent with the provisions of the order, under the supervision of FDA.

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- 2) In lieu of paragraph (c)(1) of this section, other arrangements for assuring the proper disposition of the HCT/P may be agreed upon by the person receiving the written order and FDA. Such arrangements may include, among others, providing FDA with records or other written information that adequately ensure that the HCT/P has been recovered, processed, stored, and distributed in conformance with this part, and that, except as provided under Sec. Sec. 1271.60, 1271.65, and 1271.90, the donor of the cells or tissue for the HCT/P has been determined to be eligible.

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- (d) A written order issued under paragraph (a)(3) of this section will specify the regulations with which you must achieve compliance and will ordinarily specify the particular operations covered by the order. After receipt of an order that is in effect and issued under paragraph (a)(3) of this section, you must not resume operations without prior written authorization of FDA.

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(e) The recipient of an order issued under this section may request a hearing in accordance with part 16 of this chapter. To request a hearing, the recipient of the written order or prior possessor of such HCT/P must make the request within 5 working days of receipt of a written order for retention, recall, destruction, and/or cessation (or within 5 working days of the agency's possession of an HCT/P under paragraph (a)(2) of this section), in accordance with part 16 of this chapter. An order of destruction will be held in abeyance pending resolution of the hearing request

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. Upon request under part 16 of this chapter, FDA will provide an opportunity for an expedited hearing for an order of cessation that is not stayed by the Commissioner of Food and Drugs.

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- (f) FDA will not issue an order for the destruction of reproductive tissue under paragraph (a)(1) of this section, nor will it carry out such destruction itself under paragraph (a)(2) of this section.